UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 17, 2002

MEMORANDUM

SUBJECT: EFED response to Reckitt Benckiser Inc. (Reckitt) errors-only comments on the Agency document "Comparative Risks of Nine Rodenticides to Birds and Nontarget Mammals"

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THRU: Stephanie Irene, Acting Chief
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The Environmental Fate and Effects Division (EFED) has reviewed the "errors-only" response of Reckitt Benckiser Inc. (Reckitt) to the Agency document "Comparative Risks of Nine Rodenticides to Birds and Nontarget Mammals" dated October 3, 2001. Reckitt's comments of December 7, 2001 were prepared by E. J. Moyer, Director of Regulatory Relations. As stated in the Agency's October 23, 2001 cover letter for the comparative risk assessment, the registrants' 30-day response should address only mathematical, computational, typographic, or other similar errors. Matters of policy, interpretation, or applicability of data will be addressed after the public comment period in accordance with the Agency's reregistration process for pesticides.

In response to error comments by Reckitt, other rodenticide registrants, and the Rodenticide Registrants Task Force, EFED has made necessary computational and/or typographical corrections. However, EFED notes that many comments relate to policy, interpretation, or applicability of data, and those comments will be addressed along with public comments after the 60-day public-comment period.

EPA's Comparative Document Does Not Meet the Agency's Guideline for Risk Assessment.

The preliminary document that has been prepared by EPA cannot be considered a comparative risk assessment. The document relies primarily upon discussions of the toxicological hazards of the nine compounds under consideration and the number of wildlife incidents reported to the agency. In fact, the assessment itself does not appear to meet the agency's own guidelines for ecological risk assessment.

EPA defines a true ecological risk assessment as a flexible process for organizing and analyzing data, information, assumptions and uncertainties to evaluate the likelihood of an adverse ecological effect. It "evaluates the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors." 63 *Fed. Reg.* 26846 (May 14, 1998).

An ecological risk assessment involves three stages of development – problem formulation, analysis and risk characterization. In the problem formulation phase, the risk assessors evaluate goals and select assessment endpoints, prepare a conceptual model, and develop an analysis plan. See EPA *Guidelines for Ecological Risk Assessment* (May 1998).

In the analysis phase, risk assessors evaluate exposure to stressors and the relationship between stressor levels and ecological effects. The first step in analysis is to determine the strengths and limitations of data on exposure, effects and ecosystem and receptor characteristics. Data are then analyzed to characterize the nature of potential or actual exposure and the ecological responses under the circumstances defined in the conceptual model.

In the risk characterization phase, exposure and stressor-response profiles are integrated through a risk estimation process. Risk characterization must include a summary of the assumptions, scientific uncertainties, and the strengths and limitations of the analyses. The final product is a description of the risk in which results of the integration are presented, including an interpretation of ecological adversity and descriptions of uncertainty and lines of evidence. *Guidelines for Ecological Risk Assessment* at 2-6. The assessment EPA has prepared clearly does not follow these steps in formulating the conclusions presented.

Risk is designed as the integration of toxicity and exposure. Though not stated, EPA has used a "maximum expected environmental concentration" (MEEC) in its assessment of predicted risk. The MEEC is the worst-case scenario and provides a standard measure for between study comparisons. Predicted risk is <u>not</u> actual risk. Determination of actual risk requires data on how easily a nontarget animal can gain access to a bait, how likely that animal is to eat the bait, how much is absorbed, how rapidly it is removed from the target animals body, etc. We are concerned that the Agency has not conducted this rigorous of an analysis, thus producing flawed conclusions.

The Agency has relied heavily on incident data to support the likelihood of exposure. However, it appears there has been little effort to thoroughly analyze the database to determine duplicate

reports, eliminate clearly erroneous data or identify incidents where residues of active ingredients clearly had no relationship to the death of animals. The RRTF had conducted a detailed analysis of incident data and presented the results of that analysis to the Agency. The analysis clearly showed duplication of reports, discussed liver residue results and identified incidents of healthy coyotes and kit foxes (having low residue levels in their liver) that clearly died from other causes, such as euthanasia or automobiles.

EFED response: This has been addressed in the revised document. It is well known that rodenticide baits are formulated to be lethal to rodents and a few other small mammals, and they are not selective to the target species. Although many factors influence which nontarget animals might be exposed to baits, many nontarget organisms are attracted to and consume grain-based baits. Predators and scavengers also feed on rats and mice or other target species, and they are not likely to avoid feeding on those that have eaten rodenticide bait. Thus, rodenticide baits also pose potential secondary risks. EFED believes that the potential for risks to birds and nontarget mammals is well established for some of these rodenticides.

The risk assessment is based on the available data. Registrants have not submitted the data that would be needed to assess the probability of exposure. These data have been outlined in a section on *Uncertainty and Data Needs* in the revised assessment. The methodology used is similar to that used in the Agency's "Comparative Analysis of Acute Risk From Granular Pesticides" (EPA 1992) and "A Comparative Analysis of Ecological Risks from Pesticides and Their Use: Background, Methodology, Case Study" (EPA 1998)[1]; both were reviewed by a FIFRA Scientific Review Panel. Concerning the latter analysis, the Panel noted the many scientific uncertainties in the method, yet agreed that it was a useful screening tool that provides a rough estimate of relative risk. The Panel made a number of helpful suggestions to improve the utility of the method, most of which are included here.

Risk conclusions are presented in tabular and graphical form based on two analyses of the available data. The first is a comparative ranking of the potential risk based on a comparative-analysis model, and the second is a tabular comparative rating of potential risk based on a qualitative "weight-of-evidence" assessment. Quantitative estimates of risk are used in both; however, the "weight-of evidence" assessment includes qualitative assessments of secondary risk based on mortality and other adverse effects reported in laboratory and field studies, operational control programs, and incident reports, as well as toxicokinetic data and residue levels reported in primary consumers. This approach is in concert with EPA's risk-assessment guidelines[2], where professional judgement or other qualitative evaluation

[1] See December 8-9, 1998 http://www.epa.gov/scipoly/sap/1998/index.htm

[2] See Guidelines for Ecological Risk Assessment (EPA/630/R-95/002F, 1998) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12460

techniques may be used to rank risks using categories such as low, medium, and high when exposure and effects data are limited or are not easily expressed in quantitative terms.

EPA's Comparative Document Inappropriately Applies Information Equally to all Ingredients in the Assessment.

The comparative document has done an injustice to the active ingredients assessed by implying that the results from all studies may be applied evenly and more broadly than each study's intent. We feel this is a critical error in the analysis methodology. By methodology, the secondary toxicity assessment is a meta-analysis: a study that combines the results of a number of previous studies to presumably obtain a more precise and accurate analysis of an issue. For example, the number of exposed and surviving animals in 11 laboratory studies involving 8 species are totaled and then used to arrive at an assessment of 42% mortality of birds exposed to prey deliberately poisoned with brodifacoum (Page 19). This 42% mortality value is then used in comparisons with the other rodenticides. Based on this, the conclusion is reached that for birds that brodifacoum is the most toxic of the actives.

There are four issues with this.

1. For meta-analysis to be valid, the studies between rodenticides should be comparable or made to be comparable. The report rightly points out that "Although exposure scenarios, test species, and the number of test animals vary among the studies, collectively they provide sufficient information to characterize secondary toxicity from short-term exposure" (page 19). I think that this is an overstatement. No attempt was made to make the data on actives directly comparable to each other.

2. The 'mean' mortality (eg: 42% for brodifacoum) is estimated by pooling the frequencies of the number of dead and the number of surviving animals from all studies. This means that studies within each rodenticide active do not have equal weight. Studies with larger sample sizes will contribute more to the estimate of the mean and studies, which adopt a more lethal feeding strategy, will increase the mean. The mean is a 'weighted' mean with weights provided by the study sample size. The assumption is that those studies with larger samples are more important than those with smaller sample sizes. This might not be the case: you have to take into consideration the quality of the studies. A poor study with a large sample size only produces a large amount of poor data! In the absence of any knowledge of study quality, an 'unweighted mean' would give a more unbiased estimate of mortality. An unweighted mean is calculated by determining the mortality in each study, then using these values to estimate the mean mortality between studies. Each study now makes an equal contribution to the overall mean. The unweighted mean mortality in the brodifacoum-exposed birds becomes 22.4% compared to the weighted mean of 42%; for mammals the unweighted mean is 45.4% compared to the weighted mean of 42%.

3. The laboratory studies focus very strongly on the risks of agricultural uses of the rodenticides not to use in urban areas. Predators and scavengers are exposed to very high levels of poisoned prey (eg. two or more fully dosed rodents per day for a number of days). We question the relevancy of these data for use in evaluating urban usage of rodenticides in the USA where home-owners are usually dealing with only 1-2 rodents in their home in any one year (and then, at only certain times of the year). The use of rodenticides in the poorer urban neighborhoods where the pest pressures may be relatively high ought to have few secondary poisoning concerns to wildlife.

4. The laboratory studies are absolute worse case scenarios that may have no basis on reality, except in the very rare plague events in agricultural settings. Their aim was specifically to achieve a lethal endpoint as a means of determining exactly what sort of intake is required to achieve secondary toxicity. Some studies (eg. Pank and Hirata 1976) continue exposing animals to dosed prey for even longer periods even though the data clearly suggested that further exposure was highly likely to be lethal. The use of all the data, with no appropriate vetting, over-exaggerates mortality rates.

Further examples of the inappropriate use of data are evident in the manner in which the Agency has supported the statement "…brodifacoum displayed the most toxicity and chlorophacinone and the non-anticoagulants the least." (page 19)

1. The Agency used a comparison of mortality data between actives that might not be appropriate (i.e.: biases estimates resulting from different species, methodologies, number of studies, sample sizes, etc.). Using the unweighted means: brodifacoum = 22.4%, bromadiolone = 20.7%, diphacinone = 33.3% mortality and for warfarin = 12.5%.

2. Use of two comparative studies that looked at a differing range of actives, none included all of the 9 actives relevant to the report and all included actives not registered in the US (page 26).

3. No studies on difethialone and bromethalin were found, and only 1 for cholecalciferol.

The authors make overly strong statements given the data available, and imply that brodifacoum clearly stands out from the other actives despite the preliminary nature of the data. Additionally, the document assumes equality of exposure for all active ingredients. The assumption of equality of exposure might be appropriate when assessing the risk associated with each active in isolation from field data. However, the incidence data cannot be adequately interpreted assuming equality of exposure because of the vast difference in active usage.

EFED response: This is not an errors response. EFED notes that secondary-toxicity issues were discussed at the open public meeting on rodenticides in October of 1999. The document has been modified, and where calculation errors have been identified, they have been corrected. The issues of weighting and possible correlations in the data have

been clearly addressed. EFED believes that the risk assessment presents an accurate balance of results from available reports and the contention that it is biased is unsupported. EFED invites all registrants to submit pertinent data to better characterize exposure and secondary toxicity so that the risk assessment can be refined in the future. In addition, see response to previous comment above.

EPA's Comparative Document Makes no Attempt to Conduct a Risk/Benefit Assessment.

Rodents, such as mice and rats are considered to be public health pests by EPA. To that means, rodenticide products are considered to be public health products. As such, EPA is mandated by FIFRA to consider the risk and benefits of public health pesticides (Section 2 (bb) of FIFRA). The Rodenticide Stakeholders Workgroup (RSW) acknowledged that rodenticides play a key role in mitigating public health risks and managing rodent damage and losses to property and crops. During the RSW process, presentations were given by CDC and other experts on the risks from commensal rodents. The final report of the RSW found that while there may be some risk of child exposure to rodenticides (based on numbers of incidents in the AAPCC database), the benefits of these products far outweighed the risks to children and could be managed through several means. As the Agency had all of this information, it should have included the discussion as part of the analysis.

EFED response: The Agency will be considering benefits later in the reregistration process, and the document has been modified to clarify that this is EFED's assessment of potential risks.

CONCLUSION

Reckitt Benckiser feels there are significant errors in the assessment document. These errors include technical errors as well as process errors. The Rodenticide Registrants Task Force has prepared an in-depth identification of the technical and process errors in the document. There may also be additional errors that have not been explored fully due to the limited time registrants have had to review and comment on the document. Therefore, the document should not be released for public comment until these errors are fully addressed.

Thank you for your consideration of these comments. I appreciate the cooperation given to Reckitt in light of the computer problems our company has been experiencing this week. We look forward to working with you to prepare a technically sound and comprehensive document.